REMARKS

Claims 1-25 are pending in this application. By this Amendment, claim 1 is amended to correct antecedence and distinguish over the cited references. No new matter is added by this Amendment. Support for the language added to claim 1 can be found throughout the original specification, for example in paragraph 33.

I. Double Patenting

Claims 1-25 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 13-15 of U.S. Patent No. 6,194,137. In order to obviate this rejection, Applicants file a Terminal Disclaimer herewith.

Reconsideration and withdrawal of the rejection are thus respectfully requested.

II. Rejections Under 35 U.S.C. §103(a)

A. Fahy

Claims 1-25 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 4,559,298 (hereinafter "Fahy"). This rejection is respectfully traversed.

The Patent Office alleges that Fahy teaches a method of removing an organ from vitrification comprising warming very slowly to near T_g to prevent fracture, then warming as fast as possible to T_m in order to avoid crystallization as much as possible, then reducing the concentration of cryoprotectants by perfusing with solutions contained of lower concentration of cryoprotectants until all cryoprotectants are removed. Applicants respectfully disagree with the Patent Office's assertion that Fahy teaches all of the features recited in claims 1-25.

Applicants submit that Fahy does not teach or suggest that the method for removing a tissue or organ from vitrification occurs under physiological pressure, as required in the present claims. One of ordinary skill in the art is aware that a serious obstacle to organ preservation is crystallization during warming. Fahy teaches that crystallization may be impeded by increasing the warming rate, by increasing the pressure, by increasing the solute

concentration, or by including polymer having low molecular weight solutes. See column 7, lines 37-43 of Fahy.

Fahy further teaches that at normal atmospheric pressure, the warming rate necessary to prevent crystallization is 600°C/min. See column 7, lines 45-48 of Fahy. This is clearly a much greater warming rate than required in the initial warming step of the present claims occurring at physiological pressure.

Fahy then teaches that application of 1900 atm pressure generally prevents crystallization at warming rates of 200°-300°C/min. See column 7, lines 51-56 of Fahy. Even at a pressure of 1900 atm as taught by Fahy, the warming rate is still greater than the warming rate required in the initial warming step of the present claims.

Applicants point out that Fahy uses the term "biocompatible." Although this term may appear similar to "physiological" as recited in claim 1, it is very different. Specifically, Fahy indicates that in order for a solution to be biocompatible, the solution must protect against baroinjury under vitrification conditions. In other words, the solution must be effective under high pressure conditions. This is clearly different from the normal physiological conditions disclosed in the present application. See, for example, paragraph 34 of the present specification.

Moreover, the example samples disclosed by Fahy were all vitrified and warmed under pressure. See column 6, lines 11-14 of Fahy. In fact, the example samples disclosed by Fahy were merely solution samples and not biological materials. No where does Fahy teach or suggest successful rewarming of biological samples that have been vitrified.

Applicants thus submit that Fahy does not teach or suggest that the method for removing a tissue or organ from vitrification occurs under physiological pressure at the specified warming rates, as required in claim 1.

For the foregoing reasons, Applicants submit that Fahy does not teach or suggest all of the features recited in claims 1-25. Reconsideration and withdrawal of the rejection are thus respectfully requested.

B. Pegg in view of Fahy et al.

Claims 1-22 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Pegg et al., "Fractures in Cryopreserved Elastic Arteries," Cryobiology, vol. 34, pp. 183-192 (1997), (hereinafter "Pegg") in view of U.S. Patent No. 5,962,214 (hereinafter "Fahy et al."). This rejection is respectfully traversed.

The Patent Office alleges that Pegg teaches or suggests all of the features recited in claims 1-22, except for decreasing the concentrations of the cryoprotectant during removal of the artery from vitrification. The Patent Office thus introduces Fahy et al. as allegedly teaching a method of removing an organ from vitrification comprising perfusing and/or super perfusing the organ with decreasing concentrations of cryoprotectant in a stepwise fashion. Applicants strenuously disagree with the Patent Office's allegations.

The Patent Office first alleges that Pegg teaches a method of removing an organ from vitrification. However, this statement as set forth by the Patent Office is incorrect. Pegg teaches removing an organ that has been cryopreserved by freezing, not vitrification as required in the present claims. Pegg clearly teaches that the cryopreservation was achieved by a traditional freezing method, not vitrification.

Applicants submit that one of ordinary skill in the art understands that freezing protocols and vitrification protocols for cryopreservation are very different methods. Vitrification protocols for tissues and organs utilize greater than 50% cryoprotectants, in combination with cooling and warming conditions that avoid ice formation. In contrast, freezing methods utilize much lower concentrations of cryoprotectants, such as between about 5% and 15% cryoprotectants, and ice formation is deliberately encouraged by nucleation. For

the Patent Office's convenience, Applicants herewith submit two articles that explain the difference between the freezing protocol and the vitrification protocol for cryopreservation.

As Pegg teaches a freezing protocol for cryopreservation, Applicants submit that one of ordinary skill in the art would not have looked to the method taught by Fahy et al. to modify the teachings of Pegg. Specifically, Fahy et al. teaches a vitrification protocol for cryopreservation, and a warming process associated therewith in which warming is done so as to avoid ice formation. As explained above, freezing and vitrification protocols are very different and exclusive of each other. Thus, one of ordinary skill in the art would not have modified the warming method associated with the freezing protocol for cryopreservation taught by Pegg with the warming method associated with the very different vitrification protocol for cryopreservation taught by Fahy et al.

Pegg teaches that arteries were cryopreserved in a 15% solution of dimethyl sulfoxide, and then placed in a laminated bag. See page 184, first column of Pegg. (This is clearly a freezing cryopreservation, as vitrification cryopreservation requires at least 50% cryoprotectant.) One method of thawing the arteries was to transfer the laminated bag from the liquid nitrogen to an insulated bag that maintained an air space around the artery bag and allowed it to warm in ambient air until a temperature determined by experimental design was reached. The laminated bag was then removed and immersed in a 37°C water bath. See page 184, second column of Pegg.

In contast, Fahy et al. teaches vitrification cryopreseravation (see the Title of Fahy et al.) where the organ is first warmed and then placed into a perfusion apparatus to begin cryoprotectant washout. See column 35, lines 6-18 of Fahy et al. In one embodiment, the concentration of vitrification solution (i.e., concentration of cryoprotectant) in preparing an organ for transplantation should be at least 40%. See column 35, lines 38-41 of Fahy et al.

One of ordinary skill in the art would not have combined the teachings of Pegg and Fahy et al. considering the drastically different preservation and warming processes taught by Pegg and Fahy et al. If Pegg and Fahy et al. were to have been combined as alleged by the Patent Office, the successful preservation of cells or organs in Pegg would not be assured.

Applicants thus submit that one of ordinary skill in the art would not have looked to the method of rewarming a tissue or organ cryopreserved by vitrification as taught by Fahy et al. to modify the vastly different preservation method for a tissue or organ as taught by Pegg.

For the foregoing reasons, Applicants submit that Pegg and Fahy et al., in combination or alone, do not teach or suggest all of the features recited in claims 1-22. Reconsideration and withdrawal of the rejection are thus respectfully requested.

C. **Pegg and Fahy et al., in further view of Fahy**

Claims 23-25 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Pegg and Fahy et al., in further view of Fahy. This rejection is respectfully traversed.

The Patent Office alleges that Pegg and Fahy et al. teach or suggest all of the features recited in claims 23-25, except for the cooling protocol recited in claims 23-25. However, Applicants submit that Fahy does not remedy the deficiencies of Pegg in view of Fahy et al. Specifically, Pegg teaches a freezing protocol for cryopreservation, instead of a vitrification protocol for cryopreservation as recited in the present claims. As with Fahy et al., Applicants submit that one of ordinary skill in the art would not have modified the freezing protocol taught by Pegg with the vitrification protocol taught by Fahy et al. and/or Fahy.

As discussed above, one of ordinary skill in the art would understand that the two step warming protocol for freezing cryopreservation as taught by Pegg has no bearing or relation to a two step warming protocol for vitreous cryopreservation as recited in the present claims.

Moreover, one of ordinary skill in the art would not have combined the teachings of Pegg and Fahy et al. and/or Fahy considering the drastically different cryopreservation and

warming processes taught by Pegg, and Fahy et al. and/or Fahy. If the references were to have been combined as alleged by the Patent Office, both the cryopreservation and warming protocols for the tissue or organ in Pegg would be drastically altered. One thus would not have made the alleged combination in view of these fundamentally different cryopreservation techniques.

For the foregoing reasons, Applicants submit that Pegg, Fahy et al. and Fahy, in combination or alone, do not teach or suggest all of the features recited in claims 23-25. Reconsideration and withdrawal of the rejection are thus respectfully requested.

III. Claim Objection

The Patent Office requested that claim 1 be amended to correct antecedence. Applicants have thus amended claim 1 as requested by the Patent Office.

IV. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1-25 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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Attachments:
Terminal Disclaimer
K. Brockbank et al., "Vitrification: Preservation of Cellular Implants," Topics in Tissue Engineering 2003, pp. 26.
M. J. Taylor, "Sub-zero Preservation and the Prospect of Long-Term Storage of Multicellular Tissues and Organs," Oxford University Press, pp. 360-390.

WPB:LL/can

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